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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/090,183	03/02/2002	Ralph A. Reisfeld	TSRI 829.0	4743

7590 08/26/2004

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EXAMINER	
BURKHART, MICHAEL D	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 08/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

S14-

Office Action Summary	Application No.	Applicant(s)	
	10/090,183	REISFELD ET AL.	
	Examiner	Art Unit	
	Michael D. Burkhart	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *11-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 32-34* is/are rejected.

7)☒ Claim(s) *1-10 and 32-34* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *3/2/02* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicants election without traverse of Group I (claims 1-10 and 32) and SEQ ID NOs. 5 and 6 in the reply filed on 6/2/04 is acknowledged. Applicants cancellation of claims 11-31 and addition of dependent claims 33-34 within the same document is also acknowledged.

Claim Objections

Claims 3 and 9 are objected to for being drawn to non-elected subject matter. Applicant has elected SEQ ID NOs 5 and 6, corresponding to murine Flk-1, as the subject matter to be examined. The non-elected VEGF receptor proteins (claim 3) and DNA sequences (claim 9) should be deleted.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10 and 32-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art

without undue experimentation (*United States v. Telectronics,* Inc. 8 USPQD2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is required is a conclusion reached by weighing several factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQQ2d 1400 (Fed. Cir. 1988) and include the following:

Unpredictability of the art. The art concerning DNA vaccines and the use of mouse models to assay efficacy in humans is unpredictable. DNA vaccines have not been approved for use in humans and data from human clinical trials have not shown much promise (Berzofsky, J.A. et al., J. Clin. Invest. Vol. 113: p.1515-1525, 2004, in particular see page 1519, second column). The use of attenuated bacterial vectors in human clinical trials for expression of heterologous antigens and induction of immunity to same is problematic and unpredictable (Garmory et al., FEMS Micro. Rev., Vol.26: p.339-353, 2002, see Table 1 in particular). DNA vaccines have not demonstrated any convincing efficacy in the treatment of cancer (Restifo, N.P. et al., Gene Therapy, Vol 7: p.89-92, 2000). Additionally, the translation of results in mouse models of disease to results in humans is fraught with unpredictability. See Gura, T. (Science, Vol. 278:p. 1041-1042, 1997) documenting that mouse models "...are not predictive at all" for cancer, and Steinman et al. (Science, Vol. 305: p. 197-200, 2004) discussing promising immunotherapy discoveries in mice that failed to translate to humans.

State of the art. The state of the art regarding the treatment of cancer by vaccination, while represented voluminously in the literature, is poorly developed. No DNA vaccine to date has been shown to be efficacious in this regard.

Number of working examples. Applicants have provided a working example of a DNA vaccine to treat tumors in mice. Applicants have provided no working examples of a DNA vaccine that can induce an effective human immune response to proliferating endothelial cells.

Amount of guidance. Applicants provide no direction for the claimed vaccine regarding use and efficacy in humans. The specification requires the skilled artisan to practice trial and error experimentation with human VEGF receptor sequences, delivery vectors, and adjuvants to determine which (if any) will be efficacious as claimed.

Scope of the invention. The claims are broad in nature and read on any VEGF receptor-based DNA vaccine.

Nature of the invention. The invention involves the unpredictable art of producing an effective immune response to proliferating endothelial cells in humans.

Level of skill in the art. While the level of skill in the art is high, the unpredictability of the art, lack of guidance, broad scope of the claims and poorly developed state of the art would require that undue and excessive experimentation would have to be conducted by the skilled artisan in order to practice the claimed invention.

Given the above analysis of the factors which the courts have determined are critical in determining whether a claimed invention is enabled, it must be considered that undue and excessive experimentation would have to be conducted by the skilled artisan in order to practice the claimed invention.

Conclusion

No claims are allowed.

The closest prior art is represented by the publication of the DNA sequences encoding Flk-1 (Mathews et al., PNAS USA Vol. 88: p.9026-9030, 1991 and Quinn et al., PNAS USA Vol. 90: p.7533-7537, both cited by applicants). These references teach the Flk-1 coding sequence, but not its use as a DNA vaccine.

While claims 3 and 9 recite a broad genus of VEGF receptors with about 80% homology to the claimed sequences, VEGF-2 receptors are well known in the art and individual functional domains, such as a tyrosine kinase sequence and immunoglobulin-like extracellular domains responsible for VEGF binding, have been described (see Ferrara, N. et al., Nat. Med. Vol. 9: p.669-676, 2003). Therefore, it is considered that these claims meet the written description requirement.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael D. Burkhart whose telephone number is (571) 272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael Burkhart
AU 1636

PRIMARY EXAMINER